

①
[✓] in Figure 5A, while Figure 5B depicts SEQ ID NOS: 20, 21, 62, 63, 75, 78, 80, 50, 72, 110, 89, 81, 82, 53, 43, 46, 70 and 71 respectively.

②
[✓] The paragraph beginning on page 15, line 1 has been amended as follows:

In general, a preferred zinc finger framework has the structure:

(A) $X_{0-2} C X_{1-5} C X_{9-14} H X_{3-6} H/C$ (SEQ ID NO:4)

③
[✓] The paragraph beginning on page 15, line 9 has been amended as follows:

In a preferred aspect of the present invention, zinc finger nucleic acid binding motifs may be represented as motifs having the following primary structure:

(B) $X^a C X_{2-4} C X_{2-3} F X^c X X X X L X X H X X X^b H$ - linker (SEQ ID NO:5)

-1 1 2 3 4 5 6 7 8 9

④
[✓] wherein X (including X^a , X^b and X^c) is any amino acid. X_{2-4} and X_{2-3} refer to the presence of 2 or 4, or 2 or 3, amino acids, respectively. The Cys and His residues, which together co-ordinate the zinc metal atom, are marked in bold text and are usually invariant, as is the Leu residue at position +4 in the α -helix.

⑤
[✓] The paragraph on page 16, line 18 has been amended as follows:

⑥
[✓] Preferably, the linker is T-G-E-K (SEQ ID NO:6) or T-G-E-K-P (SEQ ID NO:7).

⑦
[✓] The paragraph beginning on page 18, line 4, has been amended as follows:

⑧
[✓] Consensus zinc finger structures may be prepared by comparing the sequences of known zinc fingers, irrespective of whether their binding domain is known. Preferably, the consensus structure is selected from the group consisting of the consensus structure

D5 cont
P Y K C P E C G K S F S Q K S D L V K H Q R T H T G (SEQ ID NO:8), and the
consensus structure

P Y K C S E C G K A F S Q K S N L T R H Q R I H T G E K P (SEQ ID NO:9).

Σ✓ 2 The paragraph beginning on page 18, line 10, has been amended as follows: 2

D6
The consensuses are derived from the consensus provided by Krizek *et al.*, (1991) J. Am. Chem. Soc. 113:4518-4523 and from Jacobs, (1993) PhD thesis, University of Cambridge, UK. In both cases, the linker sequences described above for joining two zinc finger motifs together, namely TGEK (SEQ ID NO:6) or TGEKP (SEQ ID NO:7) can be formed on the ends of the consensus. Thus, a P may be removed where necessary, or, in the case of the consensus terminating T G, E K (P) can be added.

Σ✓ 2 The paragraph beginning on page 19, line 15, has been amended as follows: 2

D7
A "leader" peptide may be added to the N-terminal finger. Preferably, the leader peptide is MAEEKP (SEQ ID NO:10).

Σ✓ 2 The paragraph beginning on page 33, line 6, has been amended as follows: 2

D8
Library selections are carried out using DNA binding sites that resembled the Zif268 operator, but which contained systematic combinations of bases in the DNA doublet which forms the base-step between the DNA subsites of F2 and F3. DNA binding sites are of the generic form 5'-GNX-XCG-GCG-3' (SEQ ID NO:1), where X-X denotes a given combination of the bases at the interface between the DNA subsites, and N denotes that the four bases are equally represented at DNA position 3. Thus the interaction between F3[+3] and nucleotide position 3N is allowed complete freedom in this experiment. This feature of the library allows selection of a large family (or database) of related zinc fingers that bind a given combination of bases at nucleotide positions 4X and

D8 cont
5X, but which are non-identical owing to different interaction with the middle base in the nominal triplet subsite of F3.

[✓] The paragraph beginning on page 33, line 18, has been amended as follows:

D9
The first library to be constructed, LIB-A, contains randomizations at F2 residue position 6 and F3 residue positions -1, 1, 2 and 3 (see Figure 2), and is sorted using the DNA sequence 5'GNX-XCG-GCG-3' (SEQ ID NO:1), where X-X denotes a known combination of the two bases at DNA positions 4X and 5X, and N denotes an equal probability of any of the four bases at DNA position 3. The second library, LIB-B, contains randomizations at F2 residue position 6 and F3 residue positions -1 and 2, and is sorted using the DNA sequence 5'-GCX-XCG-GCG3' (SEQ ID NO:2), where X-X denotes a known combination of the two bases at DNA positions 4X and 5X.

[✓] The paragraph beginning on page 39, line 29, has been amended as follows:

D10
Selections are performed using the DNA sequence GCG-GMN-OPQ (SEQ ID NO:3) for LIB 1/2 and the DNA sequence IJK-LMG-GCG (SEQ ID NO:11) for LIB 2/3, where the underlined bases are bound by the WT Zif268 residues and each of the other letters stands for any given nucleotide. The conserved nucleotides of the Zif268 binding site serve to fix the register of the interaction by binding to the conserved portion of the Zif268 DNA-binding domain. The binary phage display libraries can be mixed so that selections using these two generic sites are performed in a single tube, or the selections can be performed separately. After a number of rounds of selection the two libraries are recombined to produce a chimeric DNA-binding domain that recognizes the sequence IJK-LMN-OPQ.

IN THE CLAIMS:

[2] Claim 10 has been amended as follows:

10. (Amended) A library according to any preceding claim, wherein each zinc finger has the general primary structure

(A) $X^a C X_{2-4} C X_{2-3} F X^c X X X X L X X H X X X^b H$ - linker (SEQ ID NO:5)
-1 1 2 3 4 5 6 7 8 9

Claim 15 has been amended as follows:

15. (Amended) A library according to any one of claims 10 to 14 wherein the linker is T-G-E-K (SEQ ID NO:6) or T-G-E-K-P (SEQ ID NO:7).

Claim 20 has been amended as follows:

20. (Amended) A method according to claim 19, wherein the model zinc finger is a consensus zinc finger whose structure is selected from the group consisting of the consensus structure
P Y K C P E C G K S F S Q K S D L V K H Q R T H T G (SEQ ID NO:8), and the consensus structure
P Y K C S E C G K A F S Q K S N L T R H Q R I H T G E K P (SEQ ID NO:9).

REMARKS

In the Office communication mailed January 29, 2002, the Examiner stated: "The communication filed on 3/30/01 is not fully responsive to the communication mailed 6/20/01." The communication further states that the applicant must provide a copy of the Sequence Listing in computer readable form, a paper copy of the sequence listing, and a statement that the content of the paper and computer readable copies are the same.

However, the USPTO is apparently ignoring the Substitute Sequence Listing filed October 12, 2001. Certainly, no errors have been identified in this sequence listing. While Applicant has a copy of the receipt from the USPTO (enclosed) for these